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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,822	BERENSON ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 02/27/07 is acknowledged.

Claims 1-3, 11 and 12 are pending.

In view of the amendment, filed 02/27/07 the following rejections remain:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 3, 11 and 12 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for eliminating at least a substantial portion of a clonal T cells subpopulation from a mixed population of T cells and further expanding the remaining population of T cells, comprising exposing a mixed population of T cells to surface wherein said surface has attached anti-CD3 and anti-CD28 antibodies and wherein said exposure comprising : (i) culturing said mixed population of T cells with said surface wherein the ratio of surface: cells is high (at lest 5:1) to induce apoptosis in at least a substantial portion of at least one clonal T cells and (ii) further expanding the remaining mixed population of T cells by culturing said remaining T with said surface **wherein the ration of surface: cells is low,** to stimulate the proliferation of said remaining T does not reasonably provide enablement for : a method for eliminating at least a substantial portion of a clonal T cells subpopulation from a mixed population of T cells and further expanding the remaining population of T cells, wherein the remaining mixed population of cells is exposed to **any amount** of the surface wherein said surface has attached anti-CD3 and anti-CD28 antibodies, claimed in claim 3 The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, mailed on 11/02/06.

Applicant's arguments, filed 02/27 /07 have been fully considered, but have not been found convincing.

Applicant asserts that as amended claims are enabled.

Contrary to Applicant's assertion, it is noted that as has been stated in the previous Office Action, Applicant discloses a specific method for eliminating at least a substantial portion of a clonal T cell subpopulation from a mixed population of T cells wherein a mixed population of T cells has been exposed first to anti-CD3antibody and anti-CD28 antibody attached to the bead , wherein the ratio of beads to cell is high , for example 3:1 to induce apoptosis in at least a substantial portion of a clonal T cell and further expanded the remaining T cells by exposing to **lower beads: cells ratio**, for example 1:1 (see Example 1 and 4 and Table 1 in particular).

It is noted that as amended, claims 3, 11 and 12 still reads on **any beads: cell ratio**.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1,3, 11 and 12 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of the following copending applications: 20060121005, 20050226857, 20050214942, 20050153447, 20040241162, , 20030235908,20030124122, 20030119185 ,20020119568, 20020058019 is evidenced by the disclosure of the instant specification on pages 81-83 for the same reasons set forth in the previous Office Action, mailed on 11/02/06.

While the instant and copending claims do differ in certain characteristics, the instant and copending claims appear to be drawn to the same or nearly the same method for selectively stimulating expanding of subpopulation of T cell from the mixed population comprising exposing said mixed population of T cells to a surface, wherein said surface has attached anti-Cd3 antibody- anti-CD28 antibody and wherein the ratio of surface:cells is high and then low.

As is evidenced by the disclosure of the instant specification on pages 81-83 , the exposure of a mixed population of T cells to high bead:cell ratio induces apoptosis in a portion of T cells population present in a mixed population of T cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 02/27 /07 have been fully considered, but have not been found convincing.

Applicant asserts that he will considered filing a terminal disclaimer over the cited co-pending applications once the claims in the instant application are determined to be allowable.

It is noted that none of co-pending claims of the instant application are currently allowable.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 11 and 12 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17-21 of U.S. Patent No. 6867041 as is evidenced by the disclosure of the instant specification on pages 81-83 for the same reasons set forth in the previous Office Action, mailed on 11/02/06.

While the instant and claims 17-21 of U.S. Patent No. 6867041 do differ in certain characteristics, the instant and claims 17-21 of U.S. Patent No. 6867041 appear to be drawn to the same or nearly the same method for selectively stimulating expanding of subpopulation of T cell from the mixed population comprising exposing said mixed population of T cells to a surface, wherein said surface has attached anti-Cd3 antibody- anti-CD28 antibody and wherein the ratio of surface:cells is high and then low.

As is evidenced by the disclosure of the instant specification on pages 81-83 , the exposure of a mixed population of T cells to high bead:cell ratio induces apoptosis in a portion of T cells population present in a mixed population of T cell.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's amendment, filed 02/27/07 the rejections are maintained.

The following new grounds of rejection is necessitated by the amendment filed 02/27/07.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-3 , 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,352,694 or WO'03/067221 or WO 03/024989.

US Patent '694 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells in high, i.e. 3:1 and further expanding said cells by culturing said cells with said beads at the ration of bead to cell 1:1 (see entire document, Abstract and columns 9, 19 , 20 and 28 and in particular). US Patent '694 teaches that the optimal ratio of beads to cells has to be determined and can be from 1:9 to 9:1 (see column 20 in particular). US Patent '694 teaches that exposing a mixed population of T cells to

said beads, wherein the ration of beads to cells is 3:1 would result in selective elimination of CD8+ T cells which would die by apoptosis (see column 30 and Example 15 in particular). US Patent '694 further teach that selective elimination of a subpopulation of T cells by inducing apoptosis would be useful for further expanding remaining T cells (see column 51 in particular).

WO' 221 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells in high, i.e. 10:1 and further expanding said cells by culturing said cells with said beads at the ration of bead to cell 1:1 (see entire document, Abstract and pages 24 and 25 and in particular). WO' 221 further teaches administering a composition comprising fludarabine or cyclophoshamide (see page 8 in particular) WO' 221 teaches that exposing a mixed population of T cells to said beads, wherein the ratio of bead to cell is high would result in selective expanding only CD4+ T cell (see overlapping pages 46-47).

WO' 989 teaches a method of selectively expansion of a specific subpopulation of T cells, comprising exposing a mixed population of T cells to pro-apoptotic composition (see overlapping pages 16 and 17 in particular). WO' 989 teaches the use of anti-CD3 antibody - anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells in high, i.e. 10:1 and further expanding said cells by culturing said cells with said beads at the ration of bead to cell 1:1 (see entire document, pages 26 and in particular). WO' 989 teaches that using this methodologies , i.e. exposure to high and then low beads:cell ratio, it is possible to selectively expand a selective subpopulation of T cells from the mixed T cell population (see page 50 , 53 and 75 and Table 7 on page 82 in particular).

It is noted that US Patent 6,352,694 or WO'03/067221 or WO 03/024989 does not explicitly recited a method for eliminating at least a substantial portion of T cells comprising exposing a population of cells to anti-CD3 antibody -anti-CD28 antibody attached to the beads, wherein the ratio of beads to cells is 5:1 as recited in the instant claims.

It is noted however, that the claimed ration of 5:1 is an obvious variation of the recited in US Patent 6,352,694 or WO'03/067221 or WO 03/024989 ratio of beads to cells absent of a showing of unobvious property . Moreover, it would be conventional and within the skill of the art to identify and determine the optimum ratio of beads to cell to induce apoptosis or growth inhibition. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Claims 11 and 12 are included because said functional limitation would be an obvious properties of the referenced method. It is noted that the referenced method and the claimed method each used the same anti-CD3 antibody anti CD28 antibody attached to the beads to expand the population of T cells. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

4/27/07